The Cancer Target Discovery and Development Network

RFA CA-11-010

Pre-submission Meeting

July 6, 2011, 12:30 – 14:30

Bethesda, MD

Daniela S. Gerhard, Ph.D.

Director, Office of Cancer Genomics

Conference "dos and don'ts"

The dial in number: 1-877-647-3411, PIN code: 6825846373

- **DO identify yourself (name and institution) when asking a question**
- **DO turn off the microphone when you are finished talking (attendees in Bethesda)**
- **DO keep your phone on mute to reduce background noise**
  - *6 mutes the phone; if a phone is muted *6 will "unmute"
- **DO NOT put the phone on hold since some Institutions have taped content, use mute instead**
  - **FYI-should we hear music and/or advertisements, we will have to disconnect ALL the attendees and everyone will need to call back in (the only option possible since discussion is not possible with the background noise)**

Agenda

12:30 – 12:45 p.m. CTDD Overview
Daniela S. Gerhard, Ph.D.
Director, Office of Cancer Genomics

12:45 – 1:00 p.m. Review Process
Dr. Marvin Salin
Special Review and Logistics Brach
Division of Extramural Activities

1:00 – 1:15 p.m. Grant Administration
Mr. Michael S. Zarkin
Grants Management Specialist
Office of Grants Administration

1:15 – 2:30 p.m. Q & A

https://webmeeting.nih.gov/ctd2_rfa/

Examples of NIH Investment in Large Projects of Genomic Research

Office of Cancer Genomics

- Therapeutically Applicable Research to Generate Effective Treatment (TARGET)
- The Cancer Genome Atlas (TCGA)
- Cancer Genome Anatomy Project/Cancer Genome Characterization Initiative (CGAP/CGCI)
- Genome-wide association studies (GWAS) of common and complex diseases and follow-up (~60/450 grants are cancer-related)
- Others

Data generated is made publicly available

- ~20% of NIH ARRA funded genomic projects

Molecular Characterization of Cancer is Essential but not Sufficient

- **Each tumor has hundreds to thousands genomic alterations**
  - Chromosomal changes: amplifications, deletions, translocations
  - Epigenetic changes
  - Mutations

- **Little is known about the cellular function of most genes, much less how sequence variants and mutations affect them**
  - Distinguishing initiating vs. driver vs. passenger mutations
    - Drivers are defined as genes involved in tumor maintenance
    - Evidence is accumulating that multiple subclones exist within a tumor and their frequency varies between patients
  - Genomic alterations result in cancer within specific context
    - Cell of origin
    - Other molecular alterations in genes that may have synergistic or antagonistic impact

CTD^2: A Bridge from Genomics to Therapeutics

General Information

- **Mechanism of Support: U01 Cooperative Agreement**
  - Description: To support a discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing hers/his/their specific interest and competencies.
  - 8-16 applications funded in FY2012, for a period of up to 5 years
- **Up to 2 applications from an Institution**
- **Use of de-identified human genome data: E4 exemption is required**
- **Data and Resource sharing plans are required**

Goals for the CTDD Network

- **The systematic identification of novel potential targets that may inspire future development of therapeutic applications**
  - The target candidates must be identified and characterized through exploration of the genomic and other molecular alterations
- **High throughput approaches to the identification of small molecules that can be used to study the biology of cancer types and targets**
- **As genomic data become available from TARGET, TCGA, CGCI, ICGC etc., they will be added**

  - Be nimble, flexible and open to new opportunities

Concept Examples (from RFA)

- Identification of challenging, unconventional, or rarely addressed targets such as those involved in specific protein-protein interactions, specific protein-DNA interactions, regulatory RNA functions and others
- Prediction of mechanism(s) of resistance, primary or acquired, to therapy based on patients' genetic background and cancer-specific alterations
- Determination of the complex dependencies within each cancer type and the identification of combination of targets which could be exploited for therapeutic interventions
- Exploration of targets/target combinations suitable for possible synthetic lethality-based approaches, determination of the underlying mechanisms and/or identification of biologically modulators
- Development of probes, e.g., small molecules or micro RNAs (miRNAs), that modulate the targets (and their function) in the specific cell types, and the environment, in which the cancer(s) occur

Important Dates

- **Letter of Intent to NCI** **July 22, 2011**
  - gerhardd@mail.nih.gov AND
  - soldatenkovv@mail.nih.gov
- **Application due date** **August 22, 2011**
- **Review** **November 2011**
- **Awards** **by April 2012**

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National Cancer Institute

Cancer Target Discovery and Development Network

REVIEW ASPECTS

Marvin L. Salin PhD

Scientific Review Administrator

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

RFA CA-11-010

SRO Assigned

Dr. Viatcheslav Soldatenkov

"Slava"

Email: soldatenkovv@mail.nih.gov

Phone: (301) 451-4758

KEY DATES IN CTDD APPLICATION PROCESS

- July 22, 2011: Letter of Intent
- August 22, 2011: Application Receipt@5:00 PM Local Time
- Mid-November, 2011: Review Meeting
- Mid-October, 2011: Last Minute Material Receipt
- 3 Days Post- Meeting Score Release
- 45 Days Post Meeting Summary Statement Release

LAST MINUTE SUPPLEMENTAL MATERIAL

- At Discretion of SRO
- 2 Pages PDF
- For each article accepted, you may submit only the following: Authors, institutional affiliations, title of the article, the journal that accepted it, and the expected time of publication.
- Submitted 30 Days Prior to Meeting

WHOM TO CONTACT?

- From Now till Application Submission:

  Program Staff

- After Application Submission till Application Review:

  SRO

- After Panel Review:

  Program Staff

Review Guidelines

- 5 Core Review Criteria
  - ***Significance***
  - ***Investigator***
  - ***Innovation***
  - ***Approach***
  - ***Environment***
- Additions to Each of the Core Criteria Specific for the RFA
- Core Criteria are Given Scores by Individual Reviewers (Criteria Scoring)

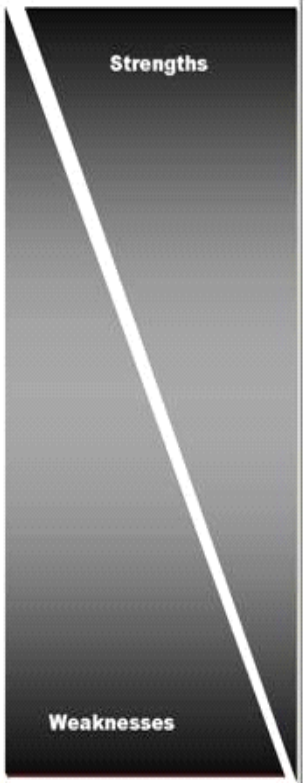
Additional Review Criteria to be Included in the Overall Score

- Protections for Human Subjects
- Inclusion of Women, Minorities and Children
- Vertebrate Animal Care and Use

Additional Non-Scoring Criteria

- Budget
- Select Agents if Appropriate
- Resource Sharing Plan

9-Point Scoring (Overall Impact)

Impact	Score	Descriptor	Strengths and Weaknesses
High Impact	1	Exceptional	
	2	Outstanding	
	3	Excellent	
Moderate Impact	4	Very Good	
	5	Good	
	6	Satisfactory	
Low Impact	7	Fair	
	8	Marginal	
	9	Poor	

Non-numeric score options: NR = Not Recommended for Further Consideration, DF = Deferred, AB = Abstention, CF = Conflict, NP = Not Present.

Additional Guidance on Strengths/Weaknesses
Exceptionally strong with essentially no weaknesses
Extremely strong with negligible weaknesses
Very strong with only some minor weaknesses
Strong but with numerous minor weaknesses
Strong but with at least one moderate weakness
Some strengths but also some moderate weaknesses
Some strengths but with at least one major weakness
A few strengths and a few major weaknesses
Very few strengths and numerous major weaknesses

LETTER FROM SRO

Sent ~ 2-3 weeks after Receipt of Applications

Contents

- Where to Find Roster
- Policy on Supplemental Material
- After Meeting Activities

RFA CA-11-010

SRO Assigned

Dr. Viatcheslav Soldatenkov

"Slava"

Email: soldatenkovv@mail.nih.gov

Phone: (301) 451-4758

Grants Management in an RFA

Office of Grants Administration

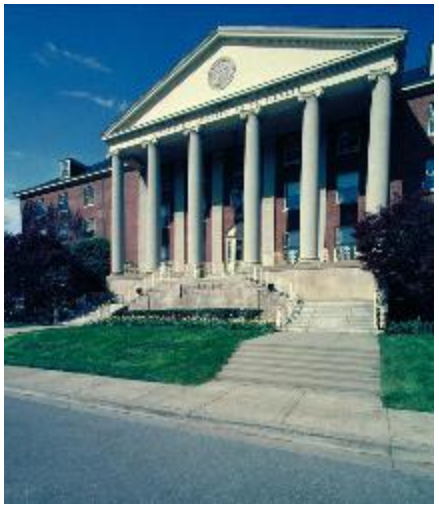
CTDD Network Pre-application Meeting

July 6, 2011

Office of Grants Administration

- a.k.a. "OGA"
- Headed by the Chief Grants Management Officer
  - Holds delegated statutory authority from the Secretary of HHS, NIH Director, and NCI Director to negotiate and make grant awards
- Staffed by Grants Management Specialists
  - Who hold delegated authority from the Chief GMO to negotiate and make grant awards
  - Overseen and supervised by Lead Specialists and Branch Chiefs
  - (And the Operations Branch which should be behind-the-scenes from a grantee's perspective.)
- OGA has sole authority to commit the NCI to a grant. No other office can make a binding promise.

A Grant is a Contract



Between the NIH and the University,

that OGA signs for the NIH,

so the investigator can complete research.

Grants vs Cooperative Agreements

- Cooperative agreements have significant ongoing government involvement in
  - Scientific activity
  - Design of project
- Other grants don't have this involvement
- Uniform Grants and Cooperative Agreements Act of 1977 governs both grants and cooperative agreements
- From the administrative perspective, cooperative agreements are no different than grants of equivalent size and complexity
- For investigators and program officers, they are quite different

Making Life Easier

- The same laws, regulations, and policies apply to these projects as to any other NCI-funded research
- Please work with Sponsored Projects in designing and submitting applications and responding to requests

Details Matter

- Up-to-date reviews
  - IRB
  - IACUC
- Other Support that demonstrates no overcommitment
- Budget justifications that explain everything
  - All costs
  - All variations and fluctuations
- Resolving IRG/study section concerns

- Please, have these items ready to go!

OGA's Activity

- Prepare, negotiate, and finalize awards
  - Only OGA can commit funds for the NCI
- Maintain the official file
  - Please copy on all significant correspondence
- Ensure regulatory compliance
  - Cost allowability, debarment, eligibility, documented reviews …
- Pre- and post-award
  - Ask us anything except scientific details

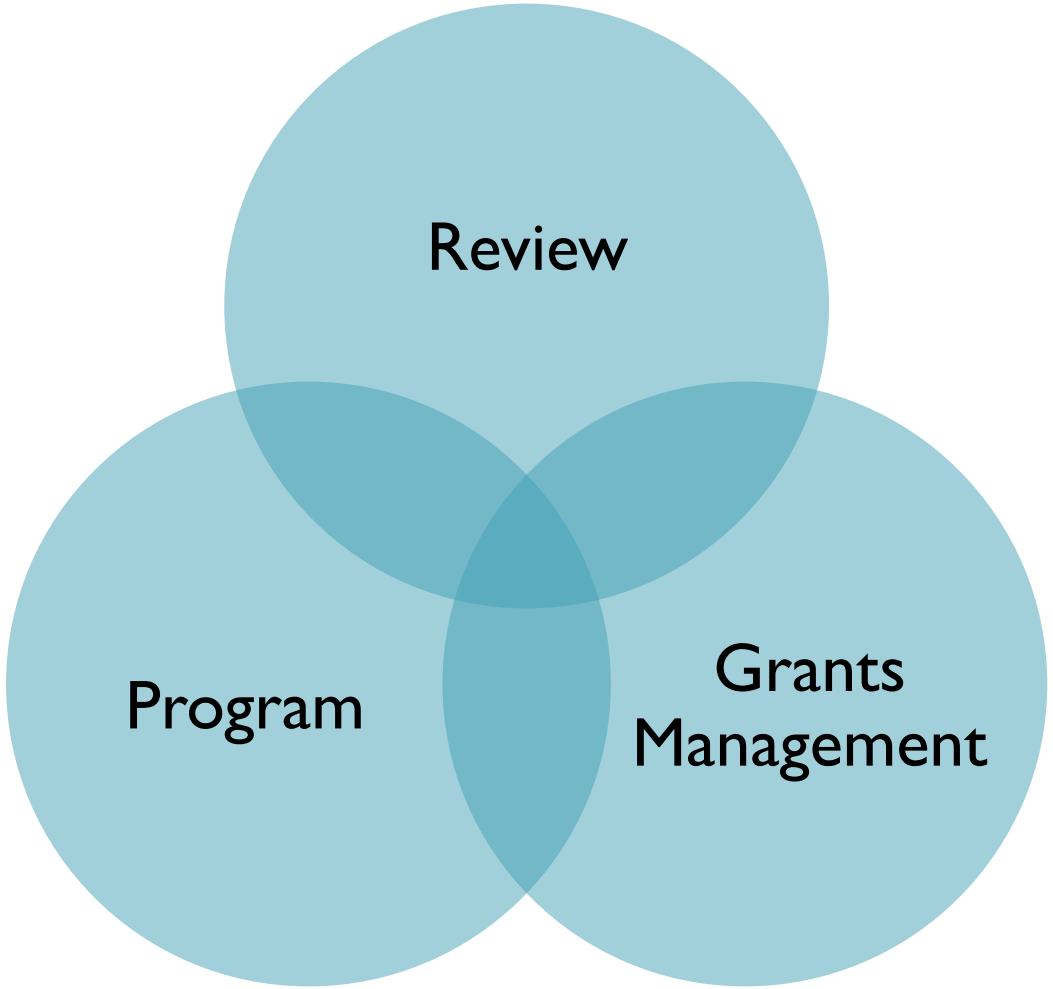
The RFA

- Details of the who (eligibility)
  - Program and Grants Management review eligibility
- Details of the what, why, and how (science)
  - Program creates and enforces these standards
- Details of the how much (funding) and when
  - Grants Management ensures compliance
  - OGA calculates the awarded budget based on the most recent negotiated rates, current legislation, annual funding plans, and other factors
  - OGA negotiates the start date for mutual convenience
- Everything in the RFA is in addition to the usually-applicable laws and regulations

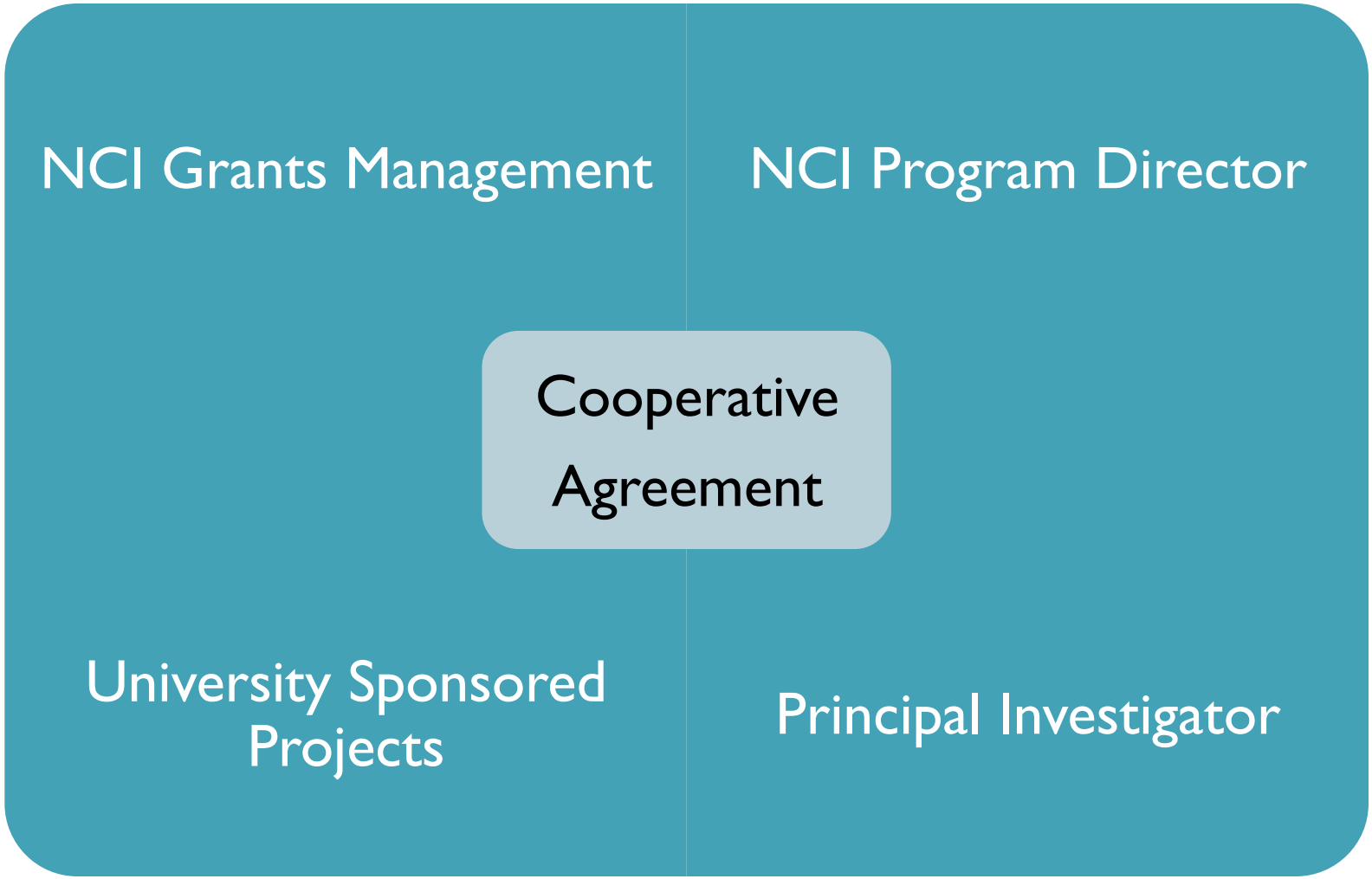
Behind the Scenes

- RFAs operate a bit differently from conventional R01 awards
  - Usually, a designated sum of money for the entire RFA
  - Divided between the selected projects
  - All of the projects funded by an RFA start at the same time
- Other than the funding, OGA will ask for the same materials we would for an R01

The Extramural Team

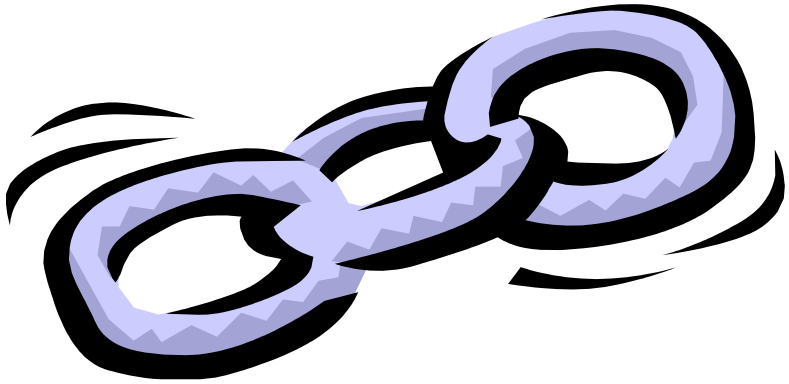


The Grants Team



Getting it done

- OGA is the last link in the chain of events before the Government commits taxpayer money to a project.
- We cannot make an award until anything involving another office is done.



The two-key system

- Before the award, initial or continuation, both Program and OGA must review the file and certify that funding is proper

- Grants Managers and Program Officers are continually discussing matters. One office will usually take the lead on a question, but please keep both sides in the loop.